

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application.

Listing of claims:

1. (Currently Amended) A method for treating diabetes which comprises administering to a mammalian species in need of treatment a therapeutically effective amount of an aP2 inhibitor, wherein the aP2 inhibitor includes **(a)** an oxazole or analogous ring selected from the group consisting of a substituted benzoyl or biphenyl-2-oxazole-alkanoic acid derivative, an oxazole derivative, a 2-thio-4,5-diphenyloxazole S-derivative, a phenyl-heterocyclic oxazole derivative, a diaryloxazole derivative, a 4,5-diphenyloxazole derivative, an oxazole carboxylic acid derivative, a phenoxyazolyloxazole derivative, or a 2-(4,5-diaryl)-2-oxazolyl substituted phenoxyalkanoic acid derivative; **and (b) a hydrogen bond donor or acceptor group and (c) an additional substituent which binds within and/or interacts with a discrete pocket within the aP2 protein defined by the amino acid residues designated Phe 16, Tyr 19, Met 20, Val 23, Val 25, Ala 33, Phe 57, Thr 74, Ala 75, Asp 76, Arg 78 in human aP2 (SEQ ID NO: 1)**.

2. (Original) The method as defined in Claim 1 wherein the aP2 inhibitor binds to the aP2 protein and inhibits its function and/or its ability to bind free fatty acids.

3-4. (Previously Cancelled)

5. Cancel.

6. (Currently Amended) The method as defined in Claim [5] **1** wherein said **additional** substituent in said aP2 inhibitor is hydrophobic in nature.

7. (Currently Amended) The method as defined in Claim [5] **1** in which the through space distance from the hydrogen bond donor/acceptor group and the additional substituent group in said aP2 inhibitor is within the distance of about 7 to about 15 Angstroms.

8. (Original) The method as defined in Claim 1 wherein Type II diabetes is treated.

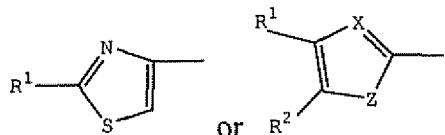
9. (Original) The method as defined in Claim 1 wherein the aP2 inhibitor is employed in the form of a pharmaceutically acceptable salt thereof or a prodrug ester thereof.

10. - 13 (Previously Cancelled)

14. (Currently Amended) A method for treating diabetes which comprises administering to a mammalian species in need of treatment a therapeutically effective amount of an aP2 inhibitor, wherein the aP2 inhibitor is selected from the group consisting of:

(I) a substituted benzoylbenzene or biphenyl alcanoic acid derivative having the structure of Formula I : $A(CH_2)_nO-B$

wherein A is a group having the formula



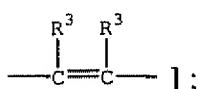
wherein

X is -N-; Z is -S- , or -O- ;

R¹ is hydrogen, lower alkyl or phenyl;

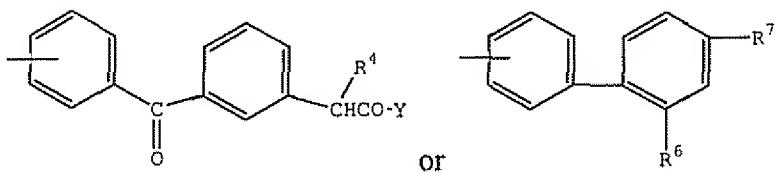
R² is hydrogen or lower alkyl; or

R¹ and R² taken together form a benzene ring [, with the proviso that when X is -N-, Z is other than



n is 1-2;

B is



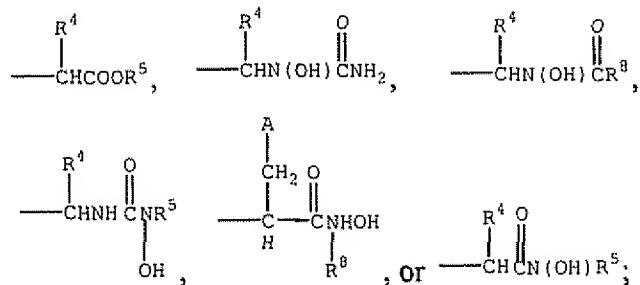
wherein

Y is OR⁵ or N(OH)R⁸;

R⁴ and R⁵ are each, independently, hydrogen or lower alkyl;

R⁶ is hydrogen, halo or nitro;

R⁷ is

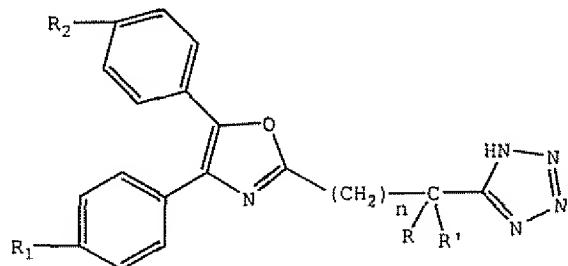


R⁸ is lower alkyl;

[m is 0-3; or a] and

pharmacologically acceptable salts thereof;

(II) oxazole derivatives which have the structure of Formula II :

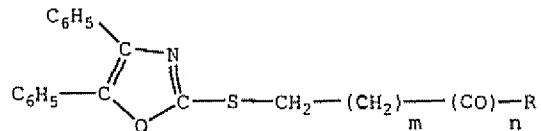


in which [;]

R and R' are identical or different and represent a hydrogen atom or an alkyl radical containing 1 or 2 carbon atoms,

R₁ and R₂ are identical or different and represent hydrogen or halogen atoms or alkoxy radicals in which the alkyl portion contains 1 to 4 carbon atoms in a straight or branched chain, and n equals 3 to 6[, as well to their salts] and pharmaceutically acceptable salts thereof;

(III) 2-thiol-4,5-diphenyloxazole S-derivatives which have the structure of Formula III :

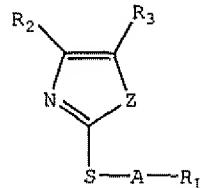


wherein m is 0, 1 or 2, n is 1 and

R represents hydroxy, alkoxy or amino, and

pharmaceutically acceptable addition salts thereof;

(IV) azole derivatives of the structure of Formula IV :



wherein

R₁ is carboxyl, esterified carboxyl or other functionally modified carboxyl group;

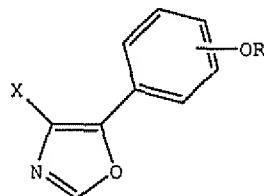
R₂ and R₃ each are aryl of up to 10 carbon atoms;

A is C_nH_{2n} in which n is an integer from 1 to 10, inclusive; [and]

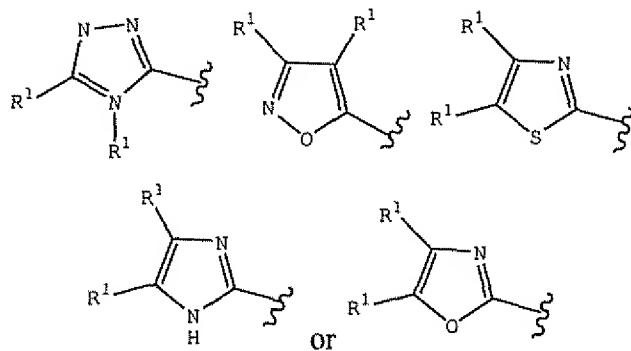
Z is O or S, and

physiologically acceptable salts thereof;

(V) phenyl-heterocyclic oxazole derivatives which have the structure of Formula V :



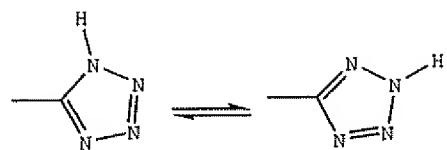
wherein X is



R is CH₂R²;

R¹ is Ph or Th;

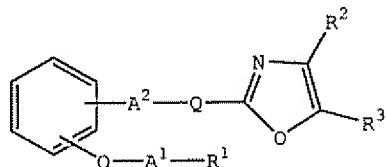
R² is



CO_2R^3 [; and] where R^3 is H, or $\text{C}_1\text{-C}_4$ lower alkyl; [or] and

pharmaceutically acceptable salt thereof;

(VI) diaryloxazole derivatives having the structure of Formula VI:



wherein R^1 is carboxy or protected carboxy,

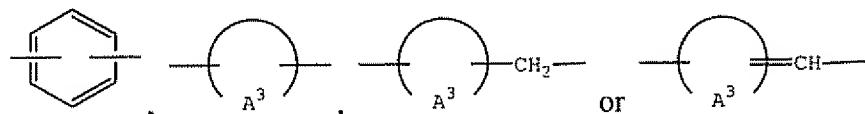
R^2 is aryl,

R^3 is aryl,

A^1 is lower alkylene,

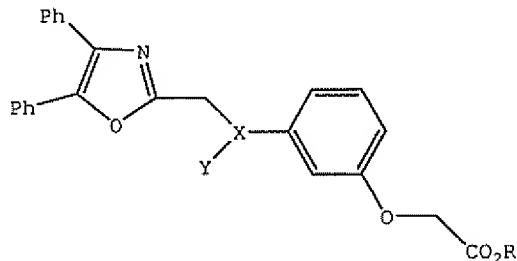
A^2 is bond or lower alkylene and

-Q- is



[() in which A^3 is cyclo (lower)alkane or cycle(lower)alkene, each of which may have [suitable] substituent(s) ()];

(VII) 4,5-diphenyloxazole derivatives having the structure of Formula VIIA:



wherein

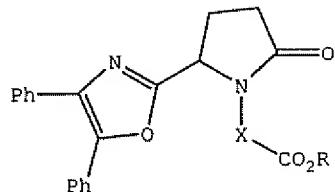
R is H or $\text{C}_1\text{-C}_5$ lower alkyl,

X is N or CH,

Y is H or CO_2R^1 , or COR^2 , provided that when X is CH, Y is not H,

R^1 is $\text{C}_1\text{-C}_5$ lower alkyl, or phenylmethyl, and

R^2 is C_1 - C_5 alkyl; or of Formula VIIIB:



wherein

R is H or C_1 - C_5 lower alkyl,

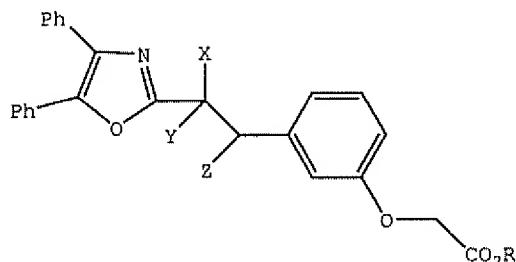
X is $(CH_2)_n$ or para or meta substituted phenyl wherein the substituent is OR^2 ,

R^2 is C_1 - C_5 alkyl, and

n is an integer of 4 to 8, and

pharmaceutically acceptable salts thereof;

(VIII) oxazole carboxylic acid derivatives having the structure of Formula VIII:



wherein

Y and Z are independently hydrogen or together form a bond;

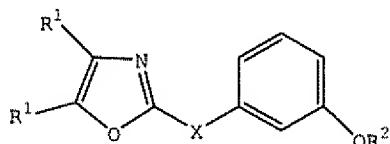
X is CN , CO_2R^1 or $CONR^2R^3$;

R and R^1 are independently or together H, Na, or C_1 - C_5 lower alkyl;

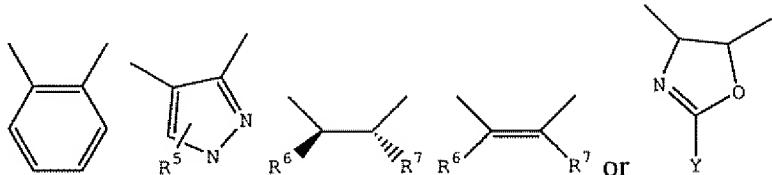
R^2 and R^3 are independently or together H, or C_1 - C_5 lower alkyl; [or] and

alkali metal salts thereof;

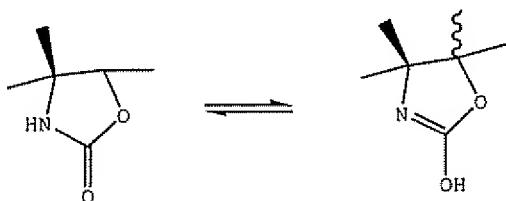
(IX) phenyloxazolyloxazole derivatives having the structure of Formula IX:



wherein X is



Y is CH₃, Ph, or OH, provided that when Y is OH, the compound exists in the keto-enol tautomerism form



R¹ is Ph or Th;

R² is CH₂R³;

R³ is CO₂R⁴;

R⁴ is H or C₁-C₅ lower alkyl;

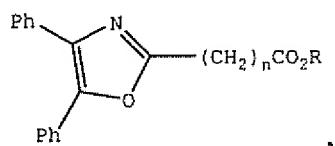
R⁵ is H or CH₃;

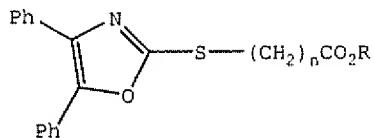
R⁶ is OHCHN or H₂N; and

R⁷ is H or OH; **[or] and**

pharmaceutically acceptable salt thereof;

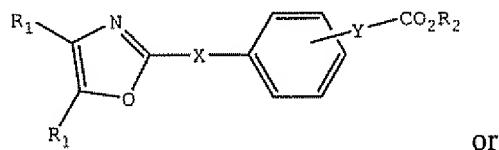
(X) 2-(4,5-diaryl)-2-oxazolyl substituted phenoxyalkanoic acids and esters having the structure **of Formula XA:**



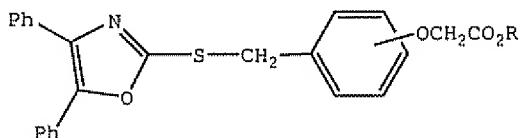
of Formula XB:

[() wherein n is 7-9 and R is hydrogen or lower alkyl; or

[when] wherein R is hydrogen, or the alkali metal salt thereof,

of Formula XC:

or

of Formula XD:

wherein

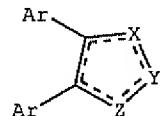
R₁ is phenyl or thienyl;

R₂ is hydrogen, lower alkyl or together with CO₂ is tetrazol-1-yl;

X is a divalent connecting group selected from the group consisting of CH₂CH₂, CH=CH, and CH₂O;

Y is a divalent connecting group attached to the 3- or 4-phenyl position selected from the group consisting of OCH₂, CH₂CH₂ and CH=CH, or when R₂ is hydrogen, an alkali metal salt thereof;

(XI) substituted 4,5-diaryl heterocycles having the structure of [f]Formula XI:

[in which] wherein

each group Ar is the same or different and is optionally substituted phenyl or optionally substituted heteroaryl;

X is nitrogen;

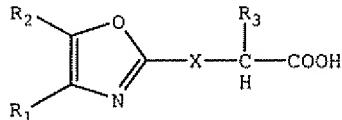
Y is C(CH₂)_nA;

Z is oxygen, and the dotted line indicates the optional presence of a double bond so as to form a fully unsaturated heterocyclic ring;

n is 4 to 12; and

A is CO_2H or a group hydrolysable to CO_2H , 5-tetrazolyl, SO_3H , $\text{P}(\text{O})(\text{OR})_2$, $\text{P}(\text{O})(\text{OH})_2$, or $\text{P}(\text{O})(\text{R})(\text{OR})$ in which R is hydrogen or $\text{C}_{1-4}\text{alkyl}$; [, or a] and pharmaceutically acceptable salts thereof;

(XII) compounds which have the structure of Formula XII:



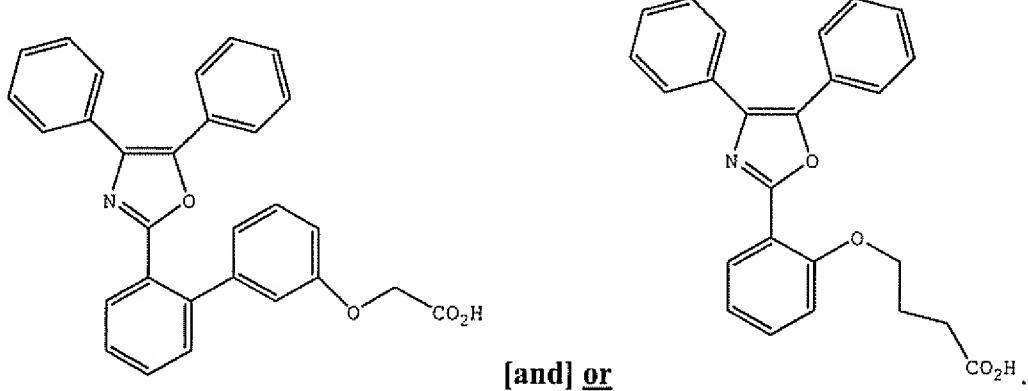
[Where] wherein X is O or S;

R_1 is H, phenyl or phenyl substituted with F, Cl or Br or alkoxy,

R_2 is H, alkyl, phenyl or phenyl substituted with F, Cl or Br or alkoxy, and

R_3 is H or alkyl.

15. (Currently Amended) The method as defined in Claim 1 wherein the aP2 inhibitor has the structure



16-20. (Previously Cancelled)